UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,652	09/05/2000	Lie-Fen Shyur	4910-8	7362

7590 12/16/2004

Cohen Pontani Lieberman & Pavane
551 Fifth Avenue
Ste 1210
New York, NY 10176

EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,652	SHYUR ET AL.	
	Examiner	Art Unit	
	Yong D Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-21,23 and 24* is/are pending in the application.

4a) Of the above claim(s) *8-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-21 and 23-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The after final amendment filed on November 3, 2004, amending claim 20, has been entered.

Claims 8-21 and 23-24 are pending. Claims 8-19 are withdrawn. Claims 20-21 and 23-24 are under consideration.

Response to Arguments

In view of the amendment filed on November 3, 2004, finality of the previous office action has been withdrawn. A new non-final rejection is set forth below.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn

Election/Restrictions

Claims 8-21 and 23-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 29, 2002.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or

specification. It is particularly noted that the sequence "PXSSSS" in claim 21 lacks a sequence identification number. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 and claim 21 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the claim, the phrase "absent the signal peptide and an amino acid sequenced of a total number of amino acid residues between 258 and 267," is confusing because it is not clear if the phrase applies to the matured wildtype enzyme or to the claimed "isolated truncated" enzyme.

Claims 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 23-24, the phrase "substantially identical" is vague. The specification defines the phrase as covering enzymes having "minor sequence variations from the specified sequences that do not affect the enzyme's enzymatic functions to any significant degrees" (pages 10-11). It is not clear as to what applicants mean by "minor

sequence variations" or "significant degrees". A standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Since the degree of modification encompassed by the phrase vague, it is also not clear if the truncated glucanase having substantial identity to SEQ ID NOs: 1 and 2 has enzymatic activity.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 20-21 are drawn to a mutant glucanase having enhanced glucanase activity relative to the matured wild type glucanase, wherein a glucanase fragment of SEQ ID NO:1 has an C-terminal extension of 1 to 19 amino acids. Therefore, the claims are drawn to a genus of glucanase variants having any structure comprising SEQ ID NO:1 and a C-terminal extension of 1 to 19 amino acids, wherein the extension comprises of any amino acids. The specification only teaches two species, the truncated glucanase of SEQ ID NOs: 1 and 2 having enhanced enzymatic activity. Two species are not enough to describe the whole genus. The specification does not describe the structure of all variants that are encompassed in the genus nor describe

which residues can be added to the C-terminus of SEQ ID NO:1 to impart the mutant with enhanced glucanase activity. Therefore, the specification fails to describe the structure of all variants of the glucanase of SEQ ID NO:1 comprising any C-terminal extension of 1-19 amino acids.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 20-21.

Claims 23-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 23-24 are drawn to a truncated glucanase having an amino acid sequence substantially identical to SEQ ID NOs: 1 or 2. Since it is not clear as to what applicants mean by "minor sequence variations" or "significant degrees" and if these variants of SEQ ID NOs: 1 and 2 have activity, the claims are drawn to a truncated glucanase having any activity. The specification does not describe the function of all polypeptides, wherein the polypeptides are derived or modified from SEQ ID NOs:1 or 2. Therefore, many functionally unrelated polypeptides are encompassed within the scope of the claims. Therefore, applicants fail to describe representative species by

identifying characteristics or functional characteristics other than being derived or modified from SEQ ID NOs: 1 or 2.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 23-24.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 20-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the glucanase of SEQ ID NOs: 1 and 2, does not reasonably provide enablement for SEQ ID NO:1 having a C-terminal extension comprising any amino acid residues. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 20-21 are drawn to a mutant glucanase having enhanced glucanase activity relative to the matured wild type glucanase, wherein a glucanase fragment of SEQ ID NO:1 has an C-terminal extension of 1 to 19 amino acids. Therefore, the claim encompasses any variants and mutants of the glucanase of SEQ ID NO:1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of glucanase variants and mutants, broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a glucanase having the amino acid sequence of SEQ ID NOs:1 and 2. It would require undue experimentation of the skilled artisan to make and use the claimed variants and mutants of SEQ ID NO:1. The specification is limited to teaching the use of a glucanase of SEQ ID NO:2 but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a

polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all mutants and variants of the glucanase of SEQ ID NO:1, because the specification does not establish: (A) amino acid residues which can be safely added to the C-terminus of SEQ ID NO:1 and result in a glucanase ha
ving enhanced glucanase activity; (B) the general tolerance of the glucanase of SEQ ID NO:1 to modification and extent of such tolerance; (C) a rational and predictable scheme for adding any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated

with the scope of the claims broadly including any variants and mutants of the glucanase of SEQ ID NO:1. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any mutants and variants of the glucanase of SEQ ID NO:1 having enhanced glucanase activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 23-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptide of SEQ ID NOs:1 and 2 having glucanase activity, does not reasonably provide enablement for a polypeptide having any activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 23-24 are drawn to a truncated glucanase having an amino acid sequence substantially identical to SEQ ID NOs: 1 or 2. Since it is not clear as to what applicants mean by "minor sequence variations" or "significant degrees" and if these variants of SEQ ID NOs: 1 and 2 have activity, the claims are drawn to a truncated glucanase having any activity. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

The function of a polypeptide cannot be predicted from its structure and the specification does not teach how to use polypeptide having any activity. The quantity of experimentation in this area is extremely large since there is significant variability in the activity of the polypeptides in the claims. It would require significant study to identify the actual function of the polypeptide and identifying a use for the polypeptide would be an inventive, unpredictable and difficult undertaking. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The art is extremely unpredictable with regard to protein function in the absence of realizable information regarding its activity. Even very similar proteins may have every different functions. In the current case, where no specific information is know regarding the function, it is entirely unpredictable what function and activity will be found for the protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the polypeptide.

Further, despite knowledge in the art for isolating polynucleotides, the specification fails to provide guidance regarding which residues of SEQ ID NOs:1 or 2 are required to encode a peptide having glucanase activity.

The specification, which places weak limitation on the structure of the polypeptides as discussed above, does not support the broad scope of the claims because the specification does **not** establish: (A) regions of the glucanase structure which may be modified that results in a peptide having glucanase activity; (B) the general tolerance of to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues resulting in a peptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use polypeptide of SEQ ID NOs: 1 and 2 but provides no guidance with regard to the making of other variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by the claims.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides having an enormous number of amino acid modifications of the polynucleotide of SEQ ID NOs: 1 or 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a polypeptide having catalytic activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935.

The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Rao Manjunath
Primary Examiner 1652
Art Unit 1652